OBITUARY NOTICES

OF

FELLOWS DECEASED.

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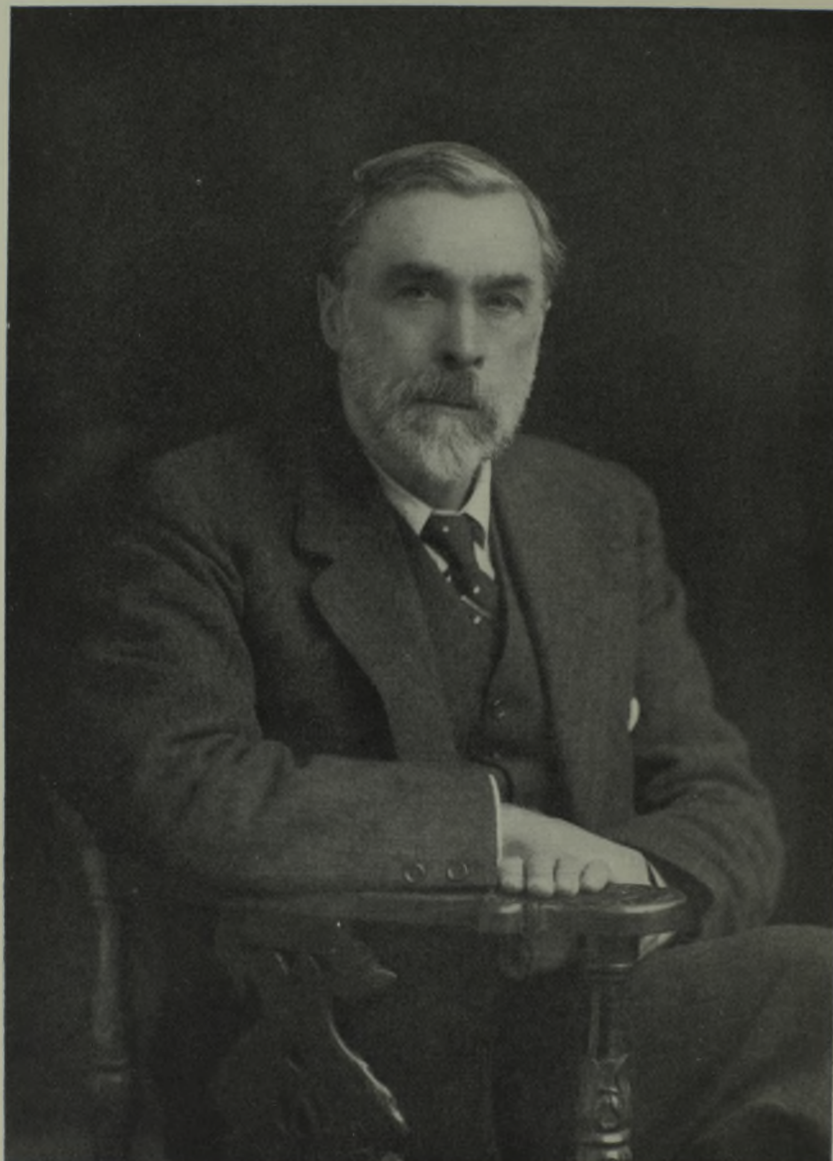
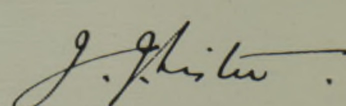




JOSEPH JACKSON LISTER—1857-1927.

The father and the grandfather of Joseph Jackson Lister were distinguished men of science and Lord Lister, the President of the Royal Society, was his uncle. With a rich inheritance of scientific talent there were combined in his character a strong love of Nature and the industry and patience to combat the handicap of a delicate constitution. He was known to his friends and colleagues as a learned and accomplished naturalist, and he acquired a world-wide reputation for his investigations on the morphology of the Foraminifera.

He was born at Leytonstone in 1857, and in his early years he and his sister used to ramble in Epping Forest guided and stimulated by their father to observe and study the animals and plants of the countryside. He soon became an ardent collector of butterflies and moths and, later on, of beetles to add to the family collections.

His father, Mr. Arthur Lister, was not only a naturalist in the ordinary sense of the term, but had inherited from his father, who had made important improvements in the compound microscope, a love for the study of minute organisms, and, acquiring an interest in the Mycetozoa, had pursued investigations on their structure and life-history which gained for him the Fellowship of the Royal Society. His son consequently was brought up in an atmosphere in which the ordinary pursuit of Natural history was supplemented by a deeper study of the problems of organic life.

Lister was sent to a school at Brighton at the age of nine, but three years later he entered the famous school of the Society of Friends at Oliver's Mount, Scarborough. The headmaster, Mr. Thomas Walton, encouraged the study of natural history, and in expeditions into the country and on the sea shore Lister added rapidly to his knowledge of wild life and to his powers of keen observation. He was not, however, only a naturalist for he took a deep interest in literature and used to enjoy reading Shakspere, Tennyson, Clough and other poets, while the writings of Carlyle were his special favourites, and from them no doubt he gained the interest in intellectual and social problems which was maintained in later years. In this respect too he was probably strongly influenced by an older relation by marriage, Mr. Joshua Rowntree, whom, in his later school days, he used to help on Sundays in an adult school for working men at Scarborough.

Lister entered St. John's College, Cambridge, in 1876, and was one of the small group of students who were fortunate enough to attend the classes of that most inspiring teacher Francis M. Balfour, at that time engaged on his wonderful investigations on the Embryology of the Chick and the Dogfish, which caused such a sensation in the scientific world. Always fond of games and naturally skilful in their pursuit Lister took to rowing as his form of exercise and relaxation at Cambridge, and in 1878 he was made stroke of the Lady Margaret boat and held that position from that time until he went to London in 1882. He led his crew to many victories both on the Cam and at Henley, and was said by a contemporary to have been the best stroke Lady Margaret had ever had.

After taking his degree in the Natural Sciences Tripos he was appointed by Prof. Newton his demonstrator in Comparative Anatomy and gave a course of lectures on the anatomy of the Vertebrata. As one of the four students who attended that course, the writer can say that it was with great regret we learned that he had decided to resign his post in order to study medicine. He then entered University College, London, as a medical student, gained the Liston gold medal in surgery and took the M.R.C.S. qualification. He was not, however, destined to practise in the profession, as his health began to fail and he was strongly urged by his uncle, Lord Lister, to spend some time in travel. He went to the West Indies with several others of his family, and on his return in the autumn of 1887 started again in a sailing ship, the *Paramatta*, on a voyage to Australia and back.

In 1887–1888 he was acting as naturalist on board H.M. Surveying Ship "Egeria," and after going to Christmas Island, Mauritius and the Seychelles, he joined the ship again in 1889 and visited Australia, New Zealand, and several islands in the Pacific. To a man of Lister's wide interests and sterling abilities these wander-years were times not only of intellectual delight but of the steady accumulation of knowledge and ideas by the direct study of Nature in her various aspects. His mind was always alert to notice things bearing on scientific theories in zoology, botany, anthropology, and geology, and he wrote several papers, to which reference will be made later, bearing on observations made during these journeys. He made his collections of animals and plants wisely and efficiently, as much for his colleagues working in the laboratories at home as to satisfy his own personal interests.

A fellow-passenger on board the *Paramatta* writes of her pleasant memories not only of the charm of his companionship during the voyage, but of his kindliness to her children, and of the interest he created by showing them through the microscope, the phosphorescent and other organisms of the ocean.

Returning to Cambridge in 1891, with his health restored, he again accepted appointments in connection with the school of zoology in the University, and also began the series of investigations on the morphology of the Foraminifera which formed the subject of his address when he was made President of Section D at the York Meeting of the British Association in 1906. In 1899 he was made a Fellow of St. John's College, and in 1900 a Fellow of the Royal Society, and for many years he was occupied with the many intellectual activities of University life in Cambridge. In various ways he improved the practical work of the school of zoology there, bringing to bear upon it his exceptionally wide knowledge and experience of living animals, both terrestrial and marine, in their natural surroundings, and his lectures were always remarkably interesting and stimulating. He continued his researches on Foraminifera and Mycetozoa, he gave valuable assistance to Adam Sedgwick in preparing the third volume of his Text-book of Zoology, in which he wrote the articles on the Crustacea and Xiphosura, and he also contributed the articles on Foraminifera and Mycetozoa in Sir Ray Lankester's Treatise on Zoology.

In 1911 he was happily married to Miss Dorothea Marryat, daughter of the late George Selwyn Marryat, and they settled down in a beautiful house in Grantchester. Some years later his health again showed signs of failure, and his visits to the zoological department became less frequent, but, turning again to the interests of his early life, he carried on at home a series of observations on the variations of butterflies and moths, though he has unfortunately left no published papers on this subject. He died in his Grantchester home on February 5, 1927.

Of Lister's published contributions to science it may be said that, although not extensive, they are valuable and interesting records of careful and skilful work done. He could never bring himself to print anything that had not been thoroughly investigated and conscientiously considered. He wrote to express the truth that he had found, and it could always be trusted, and what he has written has stood, and will stand, the test of time. His first paper was written in conjunction with Mr. J. J. Fletcher, on the female organs of reproduction of the Kangaroos, the result of some dissections he had made at the Zoological Gardens in London during the long vacation of 1881.*

In 1888† he wrote an admirable article on the Natural History of Christmas Island, the fauna and flora of which were threatened with destruction in consequence of the operations of a guano company, and in the same year he described the stalked form of the coral Fungia first discovered by Rumphius in the 17th century, and briefly described by Stutchbury in 1830.‡

Arising out of his travels in the Pacific Ocean, he wrote an account of Falcon Island,§ and of the Tonga group|| in general, in which he made important contributions to the controversy on the origin of coral reefs and to the geology of these oceanic islands. An interesting paper on the natives of Fakaofu (Bowditch Island)¶ was his only contribution to our knowledge of anthropology, but it showed that he possessed a wise insight into the problems of that science.

As a naturalist from his boyhood, he was, of course, greatly interested in the

* 'Proc. Zool. Soc.,' 1881.
† 'Proc. Zool. Soc.,' 1888.
‡ 'Quart. Journ. Micro. Sci.,' vol. xxix.
§ 'Proc. R. Geog. Soc.,' 1890.
|| 'Quart. Journ. Geol. Soc.,' 1891.
¶ 'Journ. Anthrop. Instit.,' vol. xxi.

birds of these tropical islands, and his visit to the bird colonies in the Phœnix Islands must have been one of the most thrilling incidents of his life. He published an account of the birds of this locality, including an interesting description of the throat pouch of the male Frigate bird.*

On this voyage to Australia in the *Paramatta* he spent much of his time in studying the plankton, and discovered a most interesting and hitherto unknown Metanauplius larva which he assigned, probably correctly, to the group of the Stomatopoda.†

His most important work, however, was the memoir published in the 'Philosophical Transactions' of the Royal Society in 1894 on the life-history of the Foraminifera. He described the megalo- and microspheric forms of the common *Polystomella crispa* of our shores, and showed that the microspheric form gives rise to a brood of megalospheric young, and that the megalospheric form gives rise to an immense number of minute flagellate zoospores of uniform size which in their turn give rise to the microspheric forms. He proved in this way that the two forms were not respectively male and female, as was sometimes assumed, but two distinct generations, which, in Polystomella at least, appeared to alternate. The flagellate zoospores produced by the megalospheric form might be facultative conjugants, and therefore sexual spores, but this he failed to prove. This memoir was illustrated by several excellent drawings of the living organisms, a testimony to his accuracy of observation and his delicate skill as a draughtsman.

Other papers dealing with the phenomena of dimorphism in Orbitolites, Triloculina, Biloculina, and the Nummulites were published in the 'Cambridge Philosophical Transactions,' but a great deal of valuable new work on the Foraminifera was also included in the article he wrote on the group for Lankester's 'Treatise on Zoology.' These researches brought him a great reputation, and, as Prof. F. E. Schulze, of Berlin, wrote, "won for him wide recognition among zoologists of all countries, but especially among his fellow-workers in that field of study."

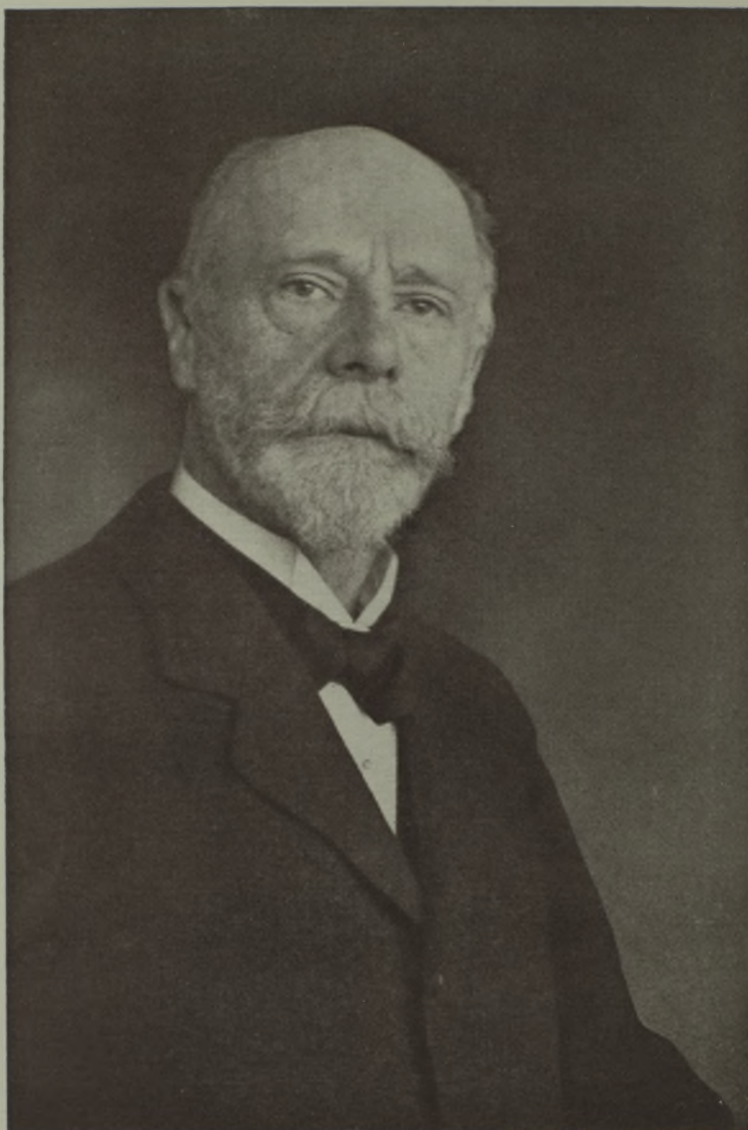
Reference may also be made to a paper he wrote in 1900 on '*Astrosclera willeyana*.'‡ He gave this name to a hard calcareous structure found by Dr. Willey on a coral reef in the South Seas, the nature of which was the subject of much speculation and of some dispute in the Laboratory. By skilled manipulation Lister settled the question through showing that the structure contained the characteristic collar-cells of a sponge.

When the Great War came upon us and zoological investigation had, to a great extent, to be set aside, Lister turned his great manual dexterity to the making of artificial limbs for wounded soldiers. He was a man who, inheriting

* 'Proc. Zool. Soc.,' 1891.

† 'Quart. Journ. Micro. Sci.,' 1898.

‡ Willey's 'Zoological Results,' Part IV.



W. Einthoven

as he did the kindliness and sympathy of his family, and having been influenced in his early life by the principles of the Society of Friends to which they belonged, must have felt keenly the horrors of war, and he did all in his power to help the sufferers.

Lister had a large number of loyal friends who held him in high regard, and there are many younger men who, having passed through their three years' course in Cambridge and gone out into the world, are grateful to him for his ever-ready help from the stores of his wide knowledge and experience, and for his sympathy in their difficulties and disappointments. S. J. H.

WILLEM EINTHOVEN—1860–1927.

Willem Einthoven, whose death was announced on 29th September, was born in May, 1860, at Samarang in Java. He was the son of a doctor practising in that place, and was taken to Holland by his mother with five other children when his father died in 1870. They settled at Utrecht, and here Einthoven entered the University as a student of medicine in 1878, to study physics under Ballot and physiology under Donders. His first research was undertaken with the anatomist Koster and concerned the mechanism of the elbow joint; he became assistant to the ophthalmologist Snellen, and was given his doctorate of medicine at 25 years for an Inaugural Dissertation entitled "Über Stereoskopie durch Farbendifferenz." In the same year he was called to the Chair of Physiology at Leyden, and there he remained, actively engaged in work, until his death in his 67th year.

Early in his career he became interested in instruments recording changes of electrical current or potential, and, perceiving their great importance to physiological research, he deliberately set out to construct an instrument of unsurpassed quickness and sensitivity. The history of the construction of his famous string galvanometer has been written by Einthoven himself in one of his papers. His researches started on the basis of the Deprez-d'Arsonval galvanometer. He soon discovered that the less numerous were the windings of the moving coil of this galvanometer, the greater was its sensitivity, and that the highest sensitivity was obtained when a single winding of very thin wire was employed. It was then (1897) that he became aware of Ader's instrument for recording submarine signals, a galvanometer consisting of a long fibre lying vertically between the poles of a magnet. He continued to enquire into the factors required to produce speed of movement and sensitivity and, by greatly increasing the strength of the magnetic field, by using relatively short and extremely fine conducting fibres, and by employing an optical system of projection of high magnification, eventually constructed a galvanometer greatly surpassing, in continued quickness of response and sensitivity, any that had previously been made.

His first account of this instrument was published in 1903; the sensitivity of the galvanometer, described fully by him in 1909, was already 100,000 times greater than that of Ader's instrument. Although his instrument, regarded as a potentiometer, then stood possessed of little more sensitivity than the best models of capillary electrometer, it surpassed the latter and all previous galvanometers enormously in the quickness of its response. The capillary electrometer had the defects of slow response and overswing; a true curve of potential differences could be obtained only by a tedious analysis of the electrometer curves, an analysis involving considerable possibilities of error. The response of Einthoven's string galvanometer was so quick that very rapid current changes were directly and accurately recorded, no analysis being required subsequently.

He expended a great deal of time and patience on the perfection not only of the galvanometer itself, but of the subsidiary apparatus, particularly plate cameras and rotating time-markers, with a view to reducing to their narrowest limits errors of measurement arising from such sources. He succeeded in reducing errors of time measurement in physiological electrical curves to such minute intervals as 1/10,000 or 1/100,000 of a second; and produced those records of current change upon a photographic network of vertical and horizontal lines, accurately representing time and current magnitude, which have commanded universal admiration for their technical perfection alone.

His galvanometer became the basis of the well-known commercial models of Edelmann, and of the Cambridge and Paul Instrument Company, and of many other patterns. Very many hundreds of these instruments are now in use in physical, physiological and pathological laboratories, and in the hospitals of many countries. Modifications, which have been introduced, other than those of the inventor himself, have consisted almost exclusively of minor changes, adapting the machine for special purposes; in principle it has remained unaltered; in sensitiveness it has greatly increased, but Einthoven's own models have continued until the last to outstrip by far all similar instruments in this respect.

Einthoven was not content merely to place his instrument at the disposal of laboratory workers; he and his collaborators clearly pointed to the many ways in which it might usefully be employed. Following up Waller's demonstration that curves of the heart beat can be obtained by leading off from the limbs of an animal, he laid the basis of human and experimental electrocardiography as these are practised to-day. Modern electrocardiography is the direct outcome of two papers published by him in 1907 and 1908. The leads from the human subject then adopted by Einthoven, and the standardisation of curves then employed by him, have since become universal. The same papers also contained curves of a variety of irregularities of the disordered or diseased heart, and their publication led at once to a complete investigation of cardiac irregularities by this method ; the outcome of these researches has been a complete and final analysis of all those irregularities that the human heart commonly displays. This work has confirmed and has widely extended the previous analyses by Mackenzie's method of studying the jugular pulse.

In 1913 he published a fundamental account, enabling the electrical axis of the human heart to be calculated at any phase of the heart's cycle ; this, by comparing the curves taken from three separate leads along the sides of an approximately equilateral triangle. This method he reduced to greater exactitude three years later, when he invented a method of recording the three leads simultaneously and accurately. The methods of these papers have been exploited extensively and fruitfully in the study of the normal heart beat and in the elucidation of the disorders of the human auricles termed flutter and fibrillation.

In other papers Einthoven showed how eminently his instrument is suited to the study of electrophysiology generally. Thus, in 1908, in illustrating its application to nerves, he showed that natural afferent impulses, conveyed by the vagus nerve from heart and lungs to brain, can be recorded ; more recently (1923) he recorded efferent impulses in the cervical sympathetic and other nerves. His methods have been extensively adopted, largely at his instigation, to study the electromotive changes in somatic nerve and muscle and in the sense organs and secretory glands.

Another and considerable activity of this pioneer was his attempt to record the sounds of the heart beat. For this purpose he used the capillary electrometer as early as 1894, in conjunction with Geluk. Later he devised a microphonic circuit suitable for attachment to his own galvanometer, wherewith sounds ranging to a vibration frequency of 200 per second might be recorded accurately. He showed this device to be suitable for registering the sounds of the human heart, and upon these he made many original observations ; it has since been used extensively to study abnormal heart sounds in patients. The heart-sound method devised by him has proved the most accurate we possess in timing the chief mechanical events in the human heart cycle, and has been much employed for this purpose. Its use has been limited, as has to a greater extent that of other devices, by inability of the instrument to follow accurately sound vibrations of very high frequency. Discovering methods of drawing out fibres to an extraordinary degree of thinness, Einthoven in his last years overcame this difficulty ; his threads of quartz, two or three millionths of an inch in diameter, would respond directly to sound vibrations of a frequency of 150,000 per second; these movements of a fibre, agitated by sound waves in the air in which it lay, Einthoven recorded photographically.

In these same, and last, years he worked to adapt his string galvanometer as a recorder for wireless waves; he succeeded in directly registering waves transmitted to Holland from the Dutch East Indies.

Einthoven's renown grew steadily, and in the last years of his life many honours were conferred upon him; these culminated in 1924 in the award of the Nobel prize for Medicine, and, in this country, in his election in 1926 to the Foreign Membership of the Royal Society. Honours, however, were to him a smaller recompense than was the knowledge of the benefits which his long and arduous work had conferred upon his fellow-men. To few scientists, perhaps to no physiologist, has the applied value of their discoveries been so abundantly demonstrated as it was to Einthoven in his lifetime; the strength of this demonstration surprised him and gave him deep satisfaction.

Einthoven's work will be remembered for all time for the greatness of its contribution to method. He himself will be remembered by those who knew him personally for his fascinating personality. A man of simple, almost humble, habits, he was untiring in his devotion to work, to the exposition of his views and to the study of related problems. He awakened in both friends and associates a profound admiration, by his genius, by the charming simplicity and directness of his character, by his unusual modesty of thought and manner, by his patience, by his natural and unfailing courtesy, and by his unswerving devotion to truth in the most exacting sense. These noble qualities endeared him to all who knew him well.

T. L.

W. B. Leishman

WILLIAM BOOG LEISHMAN—1865-1926.

WILLIAM LEISHMAN died on June 2, 1926. He was one of the small band of investigators in our Army Medical Services who, within the last 30 years, have added much to scientific knowledge and incidentally to the prestige of the Royal Army Medical Corps and Indian Medical Service. Amongst this band Leishman was distinguished, not merely for his own researches, but for his untiring and unselfish efforts to further the interests generally of medical discovery in this country.

He had a natural aptitude for scientific inquiry and found pleasure in the pursuit of knowledge and a keen interest in its practical application, but the medical service of the army was always his foremost consideration. The reputation of his corps was indeed very dear to him, and his ambition was achieved when in 1923 he became the Director of the Army Medical Service.

Leishman was born in 1865. His father, Dr. William Leishman, was Professor of Midwifery in the University of Glasgow. After a few years at Westminster School, years to which he always looked back with pleasure, Leishman started on his medical studies at Glasgow and here he graduated in 1886. Entering the army at the early age of 21, he was gazetted a Surgeon in the Medical Staff in 1887, and soon proceeded to India, where he saw active service in the Waziristan Expedition in 1894-95, receiving the frontier medal and clasp. It was characteristic of the man that, at a time when any departure from the ordinary routine of clinical work was rare, he took a microscope with him on his Indian tour.

Returning to England in 1897, he was posted as a Medical Officer to Netley Hospital, then also the Headquarters of the Army Medical School. Almroth Wright was the professor of pathology to the school, and Leishman was attracted to laboratory work under Wright's inspiration, and decided to become a serious student of pathology, if this were possible. It proved possible, and in 1900 he succeeded Major (now Sir David) Semple as Assistant Professor of Pathology at Netley.

On the removal of the Army Medical School to London and on the appointment of Sir Almroth Wright as pathologist to St. Mary's Hospital, in 1903, Leishman became Professor of Pathology at the Royal Army Medical College. For a while he was largely occupied in the organisation of the teaching of his department and his classes became an important element in the training of medical officers, both in their preliminary work on entering the army and in the "promotion courses" then made obligatory for the first time. Leishman took great pains with his teaching work and his courses of instruction were greatly appreciated. At the same time he found opportunities to do some excellent research himself and he inspired a number of young officers to undertake investigations and trained them in scientific methods.

In 1905 he was made a Brevet-Lieutenant-Colonel in recognition of his scientific investigations, and in 1910 he was elected a Fellow of the Royal Society. In 1913 he quitted his chair of pathology at the R.A.M. College to assume the duties of Expert in Tropical Diseases to the Army Medical Advisory Board at the War Office, and in the same year he became one of the original members of the Medical Research Committee.

On the outbreak of the European War, after organising the arrangements for the antityphoid inoculation of the troops proceeding overseas, he quitted the War Office for France, and in October, 1914, was made Adviser in Pathology on the Staff of the Director-General of Medical Services of the Expeditionary Force. Thrice mentioned in Despatches, he received the C.B. (Military), the Legion of Honour (3rd Class) and the American Distinguished Service Medal.

In 1918 he was recalled to the War Office and, on the formation of the new Directorates of Hygiene and Pathology, was made Director of Pathology, and in the same year he was created a K.C.M.G. In 1918, too, he was promoted to the rank of Major-General. In 1923, on the retirement of Sir John Goodwin, Leishman became Director-General, and was promoted a Lieutenant-General, created a K.C.B. and advanced by the French Government to the grade of Grand Officer of the Legion of Honour. He was also a Knight of Grace of the Order of St. John of Jerusalem.

These details will suffice to show that Leishman's accomplishments and public services were universally recognised. Let us turn now to his scientific work. In 1897, when Leishman returned from his tour of foreign service to Netley, the development of bacteriology and protozoology was proceeding apace, and the application of the new knowledge to the problems of tropical medicine was manifest. The microscope had become as important an aid to the diagnosis of tropical diseases as the clinical thermometer. His first original contribution to science, made shortly after his appointment as Assistant Professor under Wright, was an improvement in the method of staining malarial parasites so that they might be more easily detected in a film of blood. Maurer had advanced upon the methylene blue-eosin method of Romanowski by using Nocht's methylene blue ripened by alkali, but his method still involved the use of two solutions, required preliminary fixation of the film and was rather troublesome to manage.

It occurred to Leishman that by precipitating ripened methylene blue with eosin, as Jenner had done with ordinary methylene blue, a double staining compound might similarly be produced which, if also soluble in methyl alcohol, would possess the advantages of Maurer's two solutions and the conveniences of Jenner's single one. Such proved to be the case, and the useful compound stain Leishman had made came into general use for the rapid staining of microscopic preparations, of malarial parasites and other protozoa. Leishman's name became notorious all over the world amongst histologists and tropical practitioners; the chemical structure of the doubly staining compound being obscure, the name of its inventor naturally came to be attached to it.

Leishman's second piece of individual work also involved a development in scientific technique, indicating that he was capable of forging his own tools. At this time, 1900–1901, Wright had launched his experimental trial of anti-typhoid inoculation during the Boer War and was exploiting similar methods in the treatment of staphylococcic infections. This led to an investigation of the physiological mechanisms whereby the resistance occasioned by a previous injection of a killed culture of different microbes was brought about. Whereas inoculation of killed typhoid or cholera bacilli enhanced the bactericidal power of the serum, Wright found that this did not occur after the injection of staphylococci. These organisms, indeed, could be propagated in the serum of either normal or immunised animals and resistance to infection could not, therefore, be attributed to the unaided action of the serum. Wright and Leishman observed, as others had done, that in the blood of artificially immunised animals the microbes were more readily ingested by the leucocytes, but the lack of some method for estimating phagocytic activity prevented quantitative comparison.

Leishman supplied this want. His method was but roughly quantitative, but it was an important step in advance. By its use he was able to arrive at a numerical comparison of the phagocytic activity of the blood of different persons before and after they had been inoculated with killed cultures of staphylococci and *Micrococcus melitensis*, using the average number of microbes ingested by the leucocytes in the blood of a normal person as a standard of reference. He also made the interesting observation that in the case of a patient suffering from intermittent attacks of boils, a fall in this phagocytic ratio synchronised with the attack, whereas during the period of freedom from boils it was above that of normal people.

Leishman did not ascertain whether the increased phagocytic power which he observed was due to an inherent alteration in the leucocytes or to some modification in the serum which favoured the ingestion of the microbes by the phagocytes by its action upon the one or the other. He rested content with the older interpretation of Metchnikoff, that the serum was modified and stimulated the leucocytes to greater efforts, although Denys and Leclef's work had negatived this interpretation in the case of streptococci. The complete analysis of the phenomenon was subsequently made by Wright and Douglas, whose improvements in Leishman's technique permitted them to discover that it was the serum which was modified, and that microbes bathed in such modified serum were altered in such a way that they were subsequently much more readily englobed. This variable property they appropriately designated the "opsonic power" of the serum.

In their earlier experiments Wright and Douglas studied the opsonic power of the serum only of normal uninoculated persons and found that such serum lost its opsonic power after heating to 60° C. Leishman, however, discovered that the serum of individuals convalescent from Malta fever and from men who had undergone antityphoid inoculation retained its power to enhance the phagocytosis of the corresponding microbes after heating to 60°. About the same time, Neufeld and Rimpau discovered a similar thermostable opsonin in the sera of animals immunised against staphylococci and streptococci.

Leishman, therefore, opined that this thermostable property of the serum after inoculation was due to a protective substance other than the opsonins discovered by Wright and Douglas. If it was a different substance it might act in a different way; not upon the microbe but by stimulating the leucocytes themselves to greater efforts, the view originally promulgated by Metchnikoff. In 1905 Leishman published some observations designed to test this. They were not very convincing, as he was careful to point out, but they inclined him still more towards the view of the French school. He suggested the name "stimulins" for the thermostable substances in immune sera, and was rather persistent in his view that they operated upon the leucocytes, notwithstanding that evidence soon accumulated to show that the original observations of Denys and Markl had general application, and that whatever the relationship between these bodies in normal and in immune serum might be, they both increased the phagocytic power of the blood by increasing the palatability of the microbes.

It was at Netley, in 1901, that Leishman made an observation which subsequently proved of import to tropical medicine. In the course of an autopsy upon a soldier who had died of kala-azar, or "dum-dum fever," as it was then called, he examined some films of material from the spleen which he had stained by his method for malaria parasites. The field of the microscope was strewn with small oval bodies, 2-3 μ in diameter and each containing two masses of chromatin staining material, one circular and the other rod-shaped. The appearance was one he had never met with or seen described before. He did not record the observation at the time, pending opportunities for examining material from further cases of the disease, but he made careful notes and drawings of the appearance presented. Two years later, when examining specimens from rats which had died some hours previously from infection with *Trypanosoma Brucei*, he noticed degenerated trypanosomes, which so forcibly reminded him of his earlier observations that they now seemed worthy of publication. Human trypanosomiasis had been recently discovered by Dutton and Forde, so Leishman hazarded the opinion that kala-azar was a disease of similar causation, and suggested that a search for the parasites should be made in cases of the disease in India during life.

Shortly afterwards, Donovan and others recorded the observation of bodies similar to those described by Leishman in the blood from the spleen of patients suffering from kala-azar, and their universal association with the disease was soon established. Leishman's conclusion that the parasite seen by him and others was the involuted form of a trypanosome was not far from the mark, for next year, 1904, Rogers reported that he had cultivated the parasite in citrated blood outside the body, under which conditions it developed into what he at first thought to be a trypanosome. The main facts were subsequently confirmed by Leishman, but the flagellate form of the parasite turned out to be a variety of Leptomonas.

The significance of a flagellated form was not missed by Leishman, who pointed out the probability that this was the condition into which it would be found to develop in the body of some insect. The search for the insect transmitter of kala-azar has since continued, and from the work of the members of the Kala-azar Commission in India, it would appear to be a species of sand-fly (*Phlebotomus argentipes*). Successful transmission experiments by the bite of this insect have not, however, yet been accomplished, owing to the difficulty of finding a sufficiently susceptible experimental animal.

In 1904, J. H. Wright rediscovered parasites in "Delhi" boil similar to those described by Leishman, Cunningham's observations of 20 years before having been forgotten, and at the present time such parasites are known to be responsible for several diseases of men and animals. The controversy which took place over the zoological relationships of the parasites led to the conclusion that a new genus must be made for them, and, on the suggestion of Ross, the generic name, *Leishmania*, has been applied to the group.

Leishman devoted much of the time at his disposal for research after 1905 to the study of the spirochætes of relapsing fever. His earlier investigations were concerned with efforts to cultivate them and to distinguish the African from the European variety, the former being transmitted by the tick *Ornithodorus moubata*, and the latter by the body louse. All his efforts at cultivation, however, failed, and although Noguchi succeeded in 1912, Leishman was unable to repeat this. Neither by morphological characteristics nor by experiments on cross-immunisation was he able to satisfy himself of any difference between the two varieties. His experiments from 1908 onwards were directed to ascertain the life-history of the spirochæte after it was ingested by the tick, and the manner in which the infection was transmitted to man. As both monkey and mouse are susceptible to the African spirochæte, the answer to the questions could be supplied by experiments on these animals.

Koch, working in Africa in 1905, described the disappearance of the spirochætes in the stomach of the tick after a few days and their reappearance in the body fluid subsequently, and had also seen them in the ova, thus explaining the hereditary transmission of the infection in the tick. Leishman's first experiments were conducted at the temperature of a London laboratory, so that he was unable to confirm Koch's observations. He found it impossible to trace the spirochæte anywhere in the body of the tick later than the tenth day after feeding, and his search for spirochætes in the eggs laid by infected ticks proved negative. He noticed, however, that the spirochætes broke up into granules containing chromatin, and also noticed great numbers of similar granules in the bodies of some of the infected ticks.

The failure to see spirochætes, and the presence of abundant granules in ticks proved to harbour the infective agent, led Leishman to espouse the view previously enunciated by others, that these granules represented a stage in the life-history of the parasite. Later, when studying fresh tissues of infected ticks, he observed appearances which he interpreted as the growth of spirochætes from the granules. Although, on repeating his experiments at a temperature similar to that encountered in the tropics, he was able to confirm much of Koch's work, Leishman adhered to the opinion that fragmentation of spirochætes was not necessarily a degenerative process, but might represent a stage in the development of the parasite, and was probably an essential one for passing on the infection.

In his Horace Dobell Lectures to the Royal College of Physicians, in 1920, he presented the case for this opinion fairly, and stated his conclusions with moderation, pointing out that the work of Nicolle and others upon the transmission of *spirochæta recurrentis* by the body louse afforded collateral support. There is nothing inherently improbable in Leishman's view of the method, but the general consensus of opinion of parasitologists at the present time is against it.

Leishman's experiments on the means by which the infection passes from the tick to man failed to afford a decisive answer. He showed that the coxal fluid of the tick, which is often excreted by the insect whilst it is feeding, was infective, and he supposed that the parasite passed from this into the wound made by the bite, but he did not exclude a more direct method of implanting the infective agent by the insect during the act of sucking blood.

Another subject which occupied Leishman's attention was the etiology of blackwater fever. From a consideration of the epidemiology of the disease he arrived at the opinion that the view that this disease is merely a manifestation of malaria was untenable. He, therefore, took every opportunity to examine films of blood prepared from patients suffering from "blackwater," and described the occurrence therein of chromatin-staining inclusions. He inclined to believe that they represented either parasites or the reaction of the cell to the invasion of some infecting agent (chlamydozoa). Whether this be so can only be determined by further research. So far, no additional support has been forthcoming.

Leishman's biggest contribution to practical medicine was the work he did, from 1900 to 1915, to improve the efficiency and promote the practice of Wright's antityphoid inoculation in armies. When he returned to Netley Hospital in 1897, Wright had but recently introduced inoculation with a killed culture of the typhoid bacillus as a prophylactic measure. There was abundant sanction for the method from animal experiment, and its trial on troops in India under the supervision of its inventor had afforded encouraging results, but the best method of preparing a vaccine, its standardisation and the determination of the appropriate dosage still required much patient research.

As Wright's assistant, Leishman was engaged upon these researches, the first-fruits of which they published together in 1900. A method which gave promise of combating a disease which was taking a heavy toll of troops on foreign service, and which, in war, had often killed more men than the bullets of the enemy, appealed strongly to him and continued to occupy his attention for many years after the partnership with Wright ceased. The outbreak of the Boer War offered an opportunity for an extended trial of antityphoid inoculation. The permission of the War Office was obtained for the inoculation of troops as a voluntary measure, prior to their embarkation for South Africa, and the duty of preparing and standardising the vaccine for the troops was performed by Leishman.

The opinions formed as to the efficiency of antityphoid inoculation during the Boer War varied. Whilst the effect upon some units appeared to be most encouraging, in others the incidence of the disease upon inoculated and uninoculated showed little difference. The irregularity of results in different groups aroused the criticism of statisticians. It was argued that some other factors, such as variable efficiency of the vaccine used on different units, varying accuracy of diagnosis or in the records of cases, were producing an influence greater than that of inoculation. Such would appear to have been the case, for, at that time, paratyphoid diseases were not discriminated from typhoid, and no doubt a considerable proportion of the cases returned as typhoid during the Boer War were, indeed, not due to the *bacillus typhosus*. The unequal distribution of paratyphoid fevers in different units would alone be sufficient to account for the irregularities recorded.

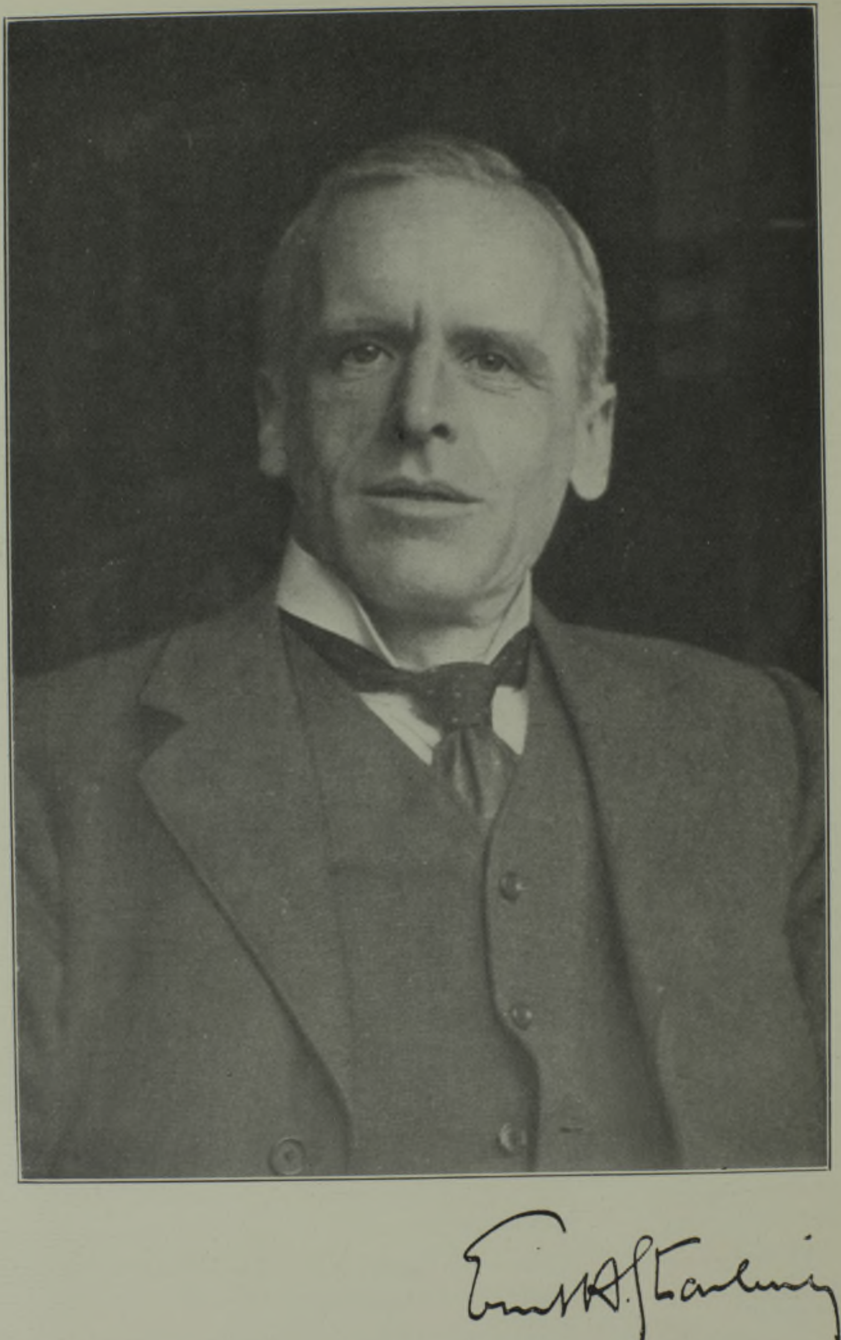
The lack of agreement upon the value of antityphoid inoculation led the Army Council, on the conclusion of the Boer War, to suspend the practice until further evidence had been collected. To secure this evidence they appointed a Departmental Committee, of which the present writer had the honour to be Chairman, to advise as to further action. After a study of the statistical and experimental evidence, this Committee presented an interim report, recommending that inoculation should be reintroduced as a voluntary measure, and that extensive experimental work should be undertaken with a view to the improvement of the system of inoculation.

A programme of research was drawn up by the Committee, and the duty of carrying out the proposed experiments devolved upon Leishman, who was a member of the Committee. The investigation proceeded in two directions: (1) the inoculation of approximately half of the individuals in all drafts proceeding to India and accurate recording of the subsequent history of both inoculated and uninoculated over a period of two years; (2) an experimental inquiry into the best method of preparing and administering the vaccine. To this end, the blood changes in animals following inoculation of the vaccine, as indicated by the amount of protective bodies aroused, were carefully and quantitatively studied in order to provide a standard method for comparison.

The inquiry occupied three years, and the credit for its successful conclusion was due to Leishman and his team of assistants. He was responsible for the details of its planning and its execution. In carrying out the programme of the Committee he showed himself to be possessed of scientific capacity of a high order and a rare administrative ability. As a result of these investigations the value of Wright's antityphoid inoculation was established beyond peradventure, a matter of deep concern when it is remembered that the medical history of all past campaigns has shown that the enteric group of diseases was as great a foe to armies on active service as the enemy.

When the European War broke out in 1914, the machinery for the immunisation of our Expeditionary Force was ready, but antityphoid vaccination was not compulsory in the British Army and, owing to the rapidity of mobilization, it was not possible to secure the inoculation of more than 25 per cent. of the troops before their embarkation for France in August, 1914. For military reasons, an attempt to remedy this defect could not be made until October, when the fighting had become localised on the Aisne. Meantime, typhoid broke out and began to spread. At this juncture, Leishman devoted himself to the task of persuading the men to be inoculated, and was extraordinarily successful. Owing to his strenuous and unremitting efforts, and those of his subordinates in the pathological service of the R.A.M.C., both at home and abroad, the proportion of inoculated soldiers on active service was increased in a couple of months to 80 per cent.; by the middle of 1915 it was 95 per cent., and by the end of the year 98 per cent. Closely following upon this successful campaign in favour of inoculation, the number of cases of typhoid fever diminished with nearly equal rapidity, and from the end of 1915 onwards was not a serious source of loss of military strength. Antityphoid inoculation does not make a man proof against the disease, but it reduces his chance of contracting it to about one-tenth, and this reduction in susceptibility was sufficient to prevent epidemic spread even under the conditions of trench warfare.

The invention of antityphoid inoculation we owe to Wright, but the successful immunization of our armies was, for the most part, due, directly and indirectly, to Leishman. By his experimental work the procedure was improved, by his



incessant propaganda the Army authorities were familiarised with the value of antityphoid inoculation, and, thanks to his tact and administrative ability, the many difficulties were overcome and the inoculation of millions of men was accomplished.

Had the casualties in the British Army from enteric fevers during 1914–18 been on the same scale as during the South African War, 900,000 of our soldiers would have been invalided, and 130,000 dead from them alone. If such a loss of man-power had occurred it must have influenced the result of the war. That the total cases were one forty-fifth and the total deaths one-hundredth of these figures is in part attributable to improvement in army sanitation, but there are good reasons for concluding that the greatest factor was the protection from epidemic extension afforded by the inoculation of almost the entire personnel of our armies. For this achievement, Leishman must be accounted to have been one of our most successful generals in the Great War.

C. J. M.

ERNEST HENRY STARLING—1866–1927.

Ernest Starling died on May 2nd, 1927, on board the *Ariguaing* shortly before reaching Kingston, Jamaica, whither he had gone on a short holiday for the benefit of his health. Of late years he had suffered from disabilities under which one of less heroic spirit could not have continued to work strenuously.

Starling was the eldest son of H. H. Starling, Clerk of the Crown at Bombay. The family of seven children had perforce to be educated in England. They therefore saw but little of their father and were brought up by their mother, an extraordinary woman, and it is to her influence by heredity and nurture that Starling owed his determination, mental alertness, and much of his charm. As the eldest boy, in the absence of a father he early acquired a sense of responsibility and capacity for managing his affairs, and was, in some respects, unusually mature for his years. He was educated at King's College School, and subsequently at Guy's Hospital.

When he began the study of the sciences preliminary to his medical education, his ambition was to be a physician, and it was not until a few years later that he contemplated the possibility of a life devoted to science and discovery.

Starling had, as a student, a brilliant academic career, about two-thirds of the academic honours available being secured by him. Physics and chemistry attracted him greatly, and the generalisation of biology, but it was when he came to study physiology that he found his real vocation, and he determined to become a physiologist, if such a career was economically possible.

After two years spent in the study of Anatomy and Physiology, he went for a few months to Heidelberg, and worked in Kühne's laboratory. He returned at the end of the year more than ever determined to become a physiologist. However, he had to put these aspirations aside for a while and apply himself to the study of practical medicine. Starling found great satisfaction and enjoyment in clinical work. The human side appealed to his sympathetic nature, and the immediate value of the application of knowledge to his practical mind. After he became a physiologist he did not lose his interest in practical medicine, and if it had been possible to devote himself wholeheartedly to the study of medicine, as is now possible by the institution of full-time professorships, Starling would have been as happy investigating disease as in a physiological laboratory. Indeed, not many years ago he seriously considered accepting such a position.

He completed his medical studies in 1889, and graduated M.D. at London in 1890, qualifying for the gold medal in medicine. Immediately after graduation he became demonstrator at Guy's Hospital, and next year, joint lecturer in physiology with Golding Bird and Washbourne.

He was now confronted with two problems. The first was how he was to continue to subsist on one-third of a salary which was never intended to command the whole services of one physiologist; the second, how he was to secure a physiological laboratory to work and teach in. A Grocers' scholarship temporarily solved the first problem, and he determined that adequate accommodation and equipment for teaching and research in physiology should, ere long, by some means, be obtained. Meanwhile, he repaired to Schafer's laboratory at University College to carry on his researches. Bayliss was also working in the laboratory, and here began a scientific partnership which lasted on and off for thirty years. The two complemented one another in many respects. Whilst both possessed scientific imagination of the highest order, Starling was more ardent and forceful, eager to translate ideas into action, but rather bored with details of technical method. He had never been interested in doing things with his hands, except climbing, although later he became a most beautiful and dexterous operator. Bayliss was the philosophical student, calm, with better critical judgment. He read widely and had a wonderful knowledge of scientific literature, was an excellent mechanic, and found enjoyment in the development of the technical methods of research. How fruitful this partnership was will be seen from the account below of Starling's scientific work.

The equipment at Guy's Hospital was steadily improved, and Starling and Bayliss did their work on the innervation of the heart together there, and Starling his on the factors controlling transudation and lymph flow, and also his earlier work on urinary secretion. By 1895 Starling had planned a really good physiological institute for Guy's Hospital, and secured the assent of the authorities to its erection. These laboratories were completed in 1897 and were, at that time, the best in London. He did not enjoy their amenities for long, as in 1899 he was appointed to the Jodrell chair of Physiology at University College.

It was a wrench to leave his new laboratories, to the planning of which he had devoted so much time, but he felt that the "atmosphere" at University College was more favourable to the realisation of his ideals. The College was, at the time, in low water financially, but he firmly believed that this temporary embarrassment could be removed, and that it need not be long before the medical sciences at University College were appropriately housed and equipped. Starling dreamed dreams, but he was also a man of action. He gave all the money he possessed to improve the equipment of the existing physiological laboratories and threw himself whole-heartedly into projects for eliminating the deficit in the College funds, and to raise the money for an Institute of Medical Sciences.

His faith was justified, and in 1909 the first instalment of his scheme came to fruition, when the present Institute of Physiology was opened, the cost of which was largely defrayed by money raised by his personal efforts. Starling's objective was not merely a new physiological school, in which he was naturally more particularly interested. He wanted all the medical sciences at University College to have the advantages of more commodious and nobler buildings. His original scheme included accommodation for anatomy and pharmacology as well as physiology, with a central library, pathology being well housed in the new Clinical School. At first only the physiological section was built, but a few years ago the erection of the whole Institute, as originally contemplated, was rendered possible by a generous gift from the Rockefeller Foundation, the directors of which were desirous of devoting funds in the interest of medical science in London. That they chose this particular means of fulfilling their aims was largely, if not entirely, due to Starling, and the noble Institute of Medical Sciences with which University College is now endowed is a fine material monument to the memory of one who not only helped to build up a great school of physiology in London and obtained an appropriate habitation for it, but also was as unsparing in his efforts to secure similar advantages for the other medical sciences.

In 1922 Starling retired from the Jodrell chair, on his appointment to a Foulerton Research Professorship of the Royal Society. This was the first of the Royal Society's professorships to be founded, and Starling was the first holder. This happy precedent has been followed and there are now five research professorships. He still continued to work at University College, but was relieved of all administrative duties and all teaching except that of a small band of research pupils. His laboratories continued to be a centre of great activity, and a limited number of distinguished young physiologists from Great Britain and abroad enjoyed the advantage of working in close communion with one of the greatest masters of experimental physiology until April, 1927.

Starling was elected a Fellow of the Society in 1899. He was Royal Medallist in 1913. He thrice served on the Council and was chairman of the Physiology and Medical Sciences Committee at the time of his death.

Starling's Physiological Researches.

Starling's interest in physiology was general, but the subjects for investigation which particularly attracted him were those physiological processes which seemed capable of interpretation in terms of chemistry and physics.

He was always, from his student days, fascinated with the problem of the heart and the adjustment of its action to varying conditions of the body, and his first paper, written with Bayliss in 1891, was on the electromotive phenomenon of the mammalian heart. Waller had recently studied the electrical variation of the excised heart, and also of the heart *in situ*, by leading off from the neighbourhood of the apex and base respectively. They believed that by photographing the movements of the capillary electrometer, connected with electrodes placed in different positions on the naked heart in the living animal, much might be learnt of the nature of the cardiac contraction ; in fact, that a new method of observation was at the disposal of the investigator. At that time, any sort of muscular continuity between the auricles and ventricles was denied, and the view that conductivity was due to some nervous network supplying the fibres was in favour.

They next explored the separate action of the vagi and accelerator nerves on the auricles, on the ventricles, and on the conducting power of the auriculo-ventricular junction in the mammal. The effects of these nerves on the hearts of frogs and tortoise had been previously studied by Gaskell and Heidenhain. Bayliss and Starling completed the story, showing that there was no essential difference between the hearts of mammals and cold-blooded animals, and that the vagus depresses conduction in auricle, auriculo-ventricular junction and ventricle, and that the accelerator nerves had the opposite effects on all three structures.

Two other important papers dealing with the mechanism of the circulation were published by Bayliss and Starling at this time. One was an exhaustive study of the simultaneous changes in the arterial and venous pressures of various regions of the body under a great variety of experimental conditions. The results showed the universal applicability of the principle of the circulation worked out by Ludwig. The other was an analysis of simultaneous pressures in the aorta and ventricles of the heart *in situ*. They used a continuous photographic record of the changes in volume of a small air-space at the end of a capillary glass tube connected with the aorta and ventricle respectively. This method being almost free from inertia and aperiodic, they succeeded in obtaining a true record of the rapid variations occurring in the ventricle and aorta and the precise relation of these to one another. Their measurements have been the standard of reference ever since.

In 1892 Starling went to work with Heidenhain in Breslau. Heidenhain had distinguished two kinds of lymphagogues, and under his inspiration Starling set to work to make a more detailed analysis of the effects of one of them, peptone. In summarising his results he adopted the interpretation of Heidenhain that the experimental facts concerning lymph formation could not be explained by filtration, and that it was necessary to suppose a selective activity on the vessel wall. On returning to England he continued to work at the problem of lymph formation and repeated all of Heidenhain's experiments. He was able to confirm his facts but came to doubt the correctness of his interpretation. He searched for evidence of lymph-secretory nerves, but found that the nervous system could only influence lymph-flow by altering vascular conditions. After years of experimenting he came to the conclusion that it was unnecessary to suppose a secretory activity of the endothelium, if some other factor existed to balance the hydrostatic pressure in the capillaries.

In 1896, Starling discovered that the missing factor required to afford a complete interpretation of the phenomena was the osmotic pressure of the colloids, to which the walls of the capillaries are relatively impermeable. It had hitherto been supposed that the osmotic pressures of proteins, being so insignificant compared to those of salts, must be of no account in physiological processes. The reverse is indeed the case, because it is only to the proteins that the membrane is impermeable. He therefore set to work to measure the osmotic pressures of the proteins in serum and found them to be, though small, of the order of magnitude of the capillary pressure. The problem was solved. The hydrostatic pressure and the osmotic pressure supplied the balance of forces necessary to explain the experimental observations.

Starling's work on lymph formation occupied five years, and is of the best he did. After long-continued and difficult experimentation, combined with observation of the highest order of accuracy, this hitherto obscure but fundamentally important region of physiology was finally illuminated by his dexterous experimentation and triumphant imagination.

Bayliss and Starling next embarked together upon an investigation on the intestinal movements and the innervation of the small and large intestine. The work was begun at Guy's Hospital and completed at University College.

When they undertook this study, the nerve supply to the small and large gut had been carefully determined by Langley and Anderson, but of the working of the neuromuscular mechanism there were many discrepancies as to fact and opinion. After eighteen months' careful experimenting, with appropriate recording methods devised for the purpose, they were able to reduce the previous chaos to order and to summarise the main facts concerning intestinal movements in a few simple statements. (1) That peristaltic contractions are true co-ordinate reflexes carried out by the local nervous mechanism and independent of the connexion with the central nervous system. (2) Local stimulation of the gut produces excitation above, inhibition below. (3) Besides the local mechanism, every part of the gut is subject to the control of the central nervous system through the splanchnics and vagi, the former being inhibitory and the latter containing both augmenting and inhibitory fibres.

This was as far as understanding of the matter progressed until Cannon introduced the method of observation by means of X-rays in an animal fed upon a bismuth meal. They next tried to find out how pancreatic secretion was brought about when food entered the duodenum. The discoveries of Pawlow had determined the order of events in gastric secretion and their co-ordination through the agency of the nervous system, but although he had found that no secretion from the pancreas occurred until the acid chyme reached the duodenum, just how pancreatic secretion was called forth had baffled this great experimenter and his pupils. Popielski had determined that the introduction of acid into the upper part of the small intestine caused secretion from the pancreas, notwithstanding previous section of the vagi and sympathetic, or even complete extirpation of the solar plexus. He concluded, therefore, that secretion must be brought about by means of some local nervous apparatus.

Bayliss and Starling started their investigations with the idea of deciding where this peripheral nervous mechanism was. They verified all the facts stated by the Russian physiologists, but they were unsuccessful in proving the existence of any nervous mechanism controlling pancreatic secretion. Nor could they discover how secretion was brought about until they made the crucial experiment which led to the discovery of secretin. I happened to be present at their discovery. In an anæsthetised dog, a loop of jejunum was tied at both ends, and the nerves supplying it dissected out and divided, so that it was connected with the rest of the body only by its blood-vessels. On the introduction of some weak hydrochloric acid into the duodenum, secretion from the pancreas occurred and continued for some minutes. After this had subsided, a few cubic centimetres of acid were introduced into the enervated loop of jejunum. To our surprise, a similarly marked secretion was produced. I remember Starling saying, "Then it must be a chemical reflex." Rapidly cutting off a further piece of jejunum, he rubbed its mucous membrane with sand in weak hydrochloric acid, filtered and injected it into the jugular vein of the animal. After a few moments, the pancreas responded by a much greater secretion than had occurred before.

Bayliss and Starling followed up their discovery in many important directions which space forbids me to mention. A method of obtaining natural pancreatic juice was now available, and they made full use of their opportunities to study trypsinogen and its conversion into trypsin by enterokinase. Starling was also moved by them to much constructive thought and further research on the chemical integration of the bodily functions generally. He proposed the name " hormones " or chemical messengers for all such active principles formed in one part of the body and distributed by the circulation to excite the normal functioning or stimulation of growth of other parts, and this term has become generally used.

In 1909, Starling returned again to the investigation of the action of the heart. He and his pupil Kawa had been attempting to dissociate the effects of asphyxia on the circulation into those due to diminished oxygen and increased carbonic acid tension respectively. They used the " spinal animal," that is, one in which the brain above the pons has been destroyed. They obtained some interesting information, but the observations were difficult to interpret without being able to separate the effects of alteration in the gaseous composition of the blood upon the heart itself.

To satisfy these requirements the heart must be isolated from the rest of the body and at the same time fed with a constant supply of perfectly oxygenated blood ; it must be working under mechanical conditions, all of which are completely under the control of the experimenter. This was accomplished by a device, now famous, known as Starling's heart-lung preparation.

This experimental device did a great deal more than serve the purpose for which it was originally designed and the years immediately succeeding the development of this method of studying cardiology were the most productive, from the point of view of scientific output, in Starling's career. He was surrounded by enthusiastic and able pupils drawn from all over the world. He had plenty of problems for them to attack, with every prospect of a reasonable reward for their efforts. Starling was unsparing in helping them towards the solution of the problem allocated to each, often performing the more difficult parts of the experiments himself and afterwards writing their papers for them.

It is only possible to indicate a few of the more fundamental facts established by this happy band of discoverers until it was scattered by the outbreak of war in 1914. Detailed accounts will be found in the publications from his laboratory between the years 1910 and 1915.

In the first case, the effects of variations in the tensions of oxygen and carbon dioxide in the blood upon the diastolic volume and output of the heart, on its capacity for work, and on the flow through the coronary arteries, were determined. The heart was found to have an astounding power of utilising the oxygen in the blood. When an isolated heart was fed with blood from an asphyxiated animal, the heart removed all but traces of oxygen. The conditions controlling the rate of the heart-beat were studied, and the only influences found to modify the rate of the isolated heart were temperature, and adrenalin. The maximum output of the heart was measured and found to be three litres a minute for a dog's heart weighing 50 gm. Observations were also made upon the energetics of the heart by Starling and Evans, and afterwards by Evans, who determined the oxygen used per unit of work done. The respiratory quotients of the normal and diabetic heart were ascertained, and from those two sets of observations the efficiency of the heart as a machine working under various loads was calculated to reach 20 per cent.

The experiments upon the flow of blood through the coronary arteries showed that this flow was primarily dependent upon the arterial pressure, but that dilatation of the coronary system occurred when the carbon dioxide tension in the blood increased, when adrenalin was added, and most markedly when some metabolites, the product of the heart's own activity, were added to the blood circulating.

The most significant of all these discoveries about the heart's action were those made by Starling and his pupils, Knowlton, Patterson and Piper, demonstrating that, within wide limits, the output of the isolated heart is independent of the rate of its beat, of the arterial pressure and of the temperature, but controlled by the inflow. This living pump, isolated from all connexions with the nervous system, is able, within wide limits, to increase its output automatically, according to the inflow, whatever the work involved.

The mechanism of this self-regulation was sought for during two years and after much ingenious experimentation, in which, later, Vischer took part, Starling and his collaborators demonstrated that there was a direct proportion between the diastolic volume of the heart and the energy set free in the following systole. The importance of this observation derives from the fact that the diastolic volume and the length of the muscle fibres are closely related, and therefore, that cardiac muscle obeys Hill's law for skeletal muscle, that the energy set free on passing from the resting to the contracted state depends upon the length of the muscle fibres.

This simple formula serves to explain the whole behaviour of the isolated mammalian heart, for, owing to this property of its muscle, if the heart fails to empty itself at one of its contractions it starts the next at greater physiological advantage.

Their researches on the heart had reached this interesting point when the European War occurred. For a few months Starling carried on his professorial work at University College, but became more and more unsettled. He wanted to go and fight. Persuaded, if not convinced, that this was not the most suitable manner in which to satisfy his strong tribal instincts, he joined the

R.A.M.C. as a Captain and was for some time a medical officer at the Herbert Hospital. Later, as the scientific resources of the country were mobilised, he was made Director of Research at the R.A.M.C. College and was busy experimenting with defensive methods against poison gases. In this he rendered invaluable service to his country. No one could have been better to control the experimental side of these researches. In 1916 he was promoted to Lt.-Colonel and sent as scientific adviser for anti-gas services to Salonika and to the Italian front. In 1917 he resigned his commission, deeming that he could be of greater service as a civilian. On his retirement he was appointed a C.M.G.

At that time food shortage seemed most likely to decide the issue, and Starling became Chairman of the Royal Society Food Committee, which was responsible for advising the Government on scientific matters fundamental to the rationing of our food supplies. He was subsequently scientific adviser to the Ministry of Food, and British scientific delegate on the Inter-Allied Food Commission. In all these capacities Starling rendered yeoman service. He soon had a mastery of the necessary facts, and he was by nature and training able to marshal them comprehensively and arrive at definite conclusions. At the same time, he realised to the full that in applying physiological principles to administrative action, the economic side of the problem was of equal or greater importance; consequently, he impressed all those statesmen and officials with whom he had to deal as one possessing, not only great knowledge, but sound judgment. It is doubtful whether any other of our physiologists could have served us so well.

For a while, after the War, Starling's work was seriously curtailed owing to ill health, which finally necessitated a serious surgical operation. However, in 1920, he was back again at work, with Anrep, on the central and reflex regulation of the circulation, using a cross-circulation method, built up on his heart-lung preparation in which the circulation through the brain of the animal was entirely under the control of the experimenter, while the animal's own heart supplied the rest of its body. By this ingenious experimentation, they were able to ascertain how the circulation in other parts of the body is modified in accordance with changes in the circulation in the brain.

After this Starling ceased for a while his experiments on the heart and turned his attention to other matters, and during the last five years of his life was mostly occupied in attempting to solve some of the many perplexities of renal secretion. It was not for the first time that he turned his attention to this subject. His experiments in 1899 had indicated that the glomerular epithelium was a simple filtering membrane, resembling a film of gelatine in permeability, whereas active secretion took place in the epithelium of the tubules. He abandoned the subject at that time, because he could see no chance for further advance until experiments could be made upon a functionally active kidney separated from the body and with some of the many factors controlling urinary secretion under experimental control.

Many attempts to achieve the necessary experimental conditions had failed, but the heart-lung preparation afforded a means by which any isolated organ might be fed with arterial blood of known composition at any desired pressure, rate of flow, and temperature. It was thus possible to study the functions of an organ apart from nervous influences and from the chemical influences which arose in consequence of modifications in the blood caused by other organs of the body. After numerous attempts, Starling and Verney succeeded in maintaining the isolated kidney in such a condition that it would secrete abundant urine.

By this method, which demands extraordinary experimental skill, Starling has opened a new chapter on the physiology of renal secretion. Already, many new facts, and others which were previously only matters of surmise, have been discovered and established. His observations with Verney and in collaboration with Eichholtz have shown that the glomeruli filter from the blood plasma its non-protein constituents, and that by using hydrocyanic acid to suspend tubular activity, a pure glomerular filtrate is obtained from the ureter. Also that, whilst urea and sulphate are secreted by the tubule cells, water, chloride, bicarbonate and glucose are re-absorbed by the tubule cells from the glomerular filtrate. Pituitrin increases the amount of chloride and decreases the amount of water eliminated.

The influence of the pituitary gland upon the secretion of the kidney was particularly studied by Starling's pupils, Eichholtz and Bruhl. Their experiments suggest that the inability of the isolated kidney to secrete inorganic phosphate is due to the absence of the pituitary hormone. If this be so, it is another discovery of a chemical correlation of the body, for which Starling is largely responsible.

These researches on the isolated kidney were in full swing in April when Starling left for the holiday which was long overdue. They were affording most promising results, and doubtless, had he been spared to continue them, he would, with his unrivalled experimental skill, ultimately have succeeded in clarifying our knowledge of urinary secretion, as he had laid bare the principles involved in the self-adjustments of the heart to physiological requirements.

Starling's influence upon physiology is not confined to his own contributions to knowledge. He was also a great exponent of the science he loved so well. His "Principles of Human Physiology" is widely read on both sides of the Atlantic and generally regarded as the best exposition of the subject in the English language. The more limited audience of his own class rooms found in him a stimulating teacher whose enthusiasm was infectious. His research pupils idolized him. To everyone, provided he were a serious inquirer after truth, he extended his help, encouragement and friendship.

Starling was the recipient of many academic honours. Honorary degrees were conferred upon him by the Universities of Dublin, Sheffield, Cambridge, Breslau, Strasburg and Heidelberg. He received the Baly Medal in 1907 and the Royal Medal in 1913. No account of his career would be complete without allusion to the part played in it by his wife. In 1891 he married Florence Wooldridge, the daughter of Sir Edward Sieveking. They were inseparable companions. With unselfish devotion she helped him more than will ever be known. They were fellow conspirators in all his projects, and for many years she performed for him the functions of an efficient secretary.

What place amongst the great discoverers in medical science should be allotted to Starling must be left to the judgment of posterity, but it will be generally conceded by his contemporaries that he was one of the foremost physiologists of our time, and that no one since Harvey has so greatly advanced our knowledge of the action of the heart.

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